Linoleic Acid Metabolites and Transepidermal Water Loss in Children With Atopic Dermatitis

**PURPOSE OF THE STUDY.** To investigate whether n-6 essential fatty acid (EFA) deficits account for atopic dermatitis (AD) by affecting transepidermal water loss (TEWL).

**STUDY POPULATION.** Children between the ages of 2 and 17 years with AD (*n* = 35), asthma or allergic rhinitis (AS/AR group, *n* = 35), or no atopic disease (*n* = 31) were studied. The AD group did not have allergic airway disease.

**METHODS.** Synthesis of the n-6 EFA from linoleic acid (LA) involves alternating steps of desaturation and elongation with serial conversion to γ-linolenic acid (GLA), dihomomo-γ-linolenic acid (DGLA), and arachidonic acid (AA). Fasting blood samples were obtained with immediate serum separation and freezing to prevent changes in fatty acid composition of serum lipids. Analysis of lipid content was performed by gas chromatography/mass spectrometry. Measurement of TEWL on the right volar forearm was reported as loss of grams of water per square meter of skin per hour. Nonparametric tests were used to evaluate differences between the groups.

**RESULTS.** Although not statistically significant, patients in the AD and AS/AR groups had higher LA and lower AA levels than controls. Patients with AD but not AS/AR had statistically lower GLA (*P* = .04) and DGLA (*P* = .03) levels than control subjects. There were no differences between the 2 groups of atopic patients. Ratios of GLA/LA, DGLA/LA, and AA/LA were lower in the AD group than controls (*P* < .01 for each). However, in the AS/AR group, only the GLA/LA and DGLA/LA ratios were statistically lower than in controls. TEWL had a significant negative correlation with GLA and DGLA (*P* = .001) and near-significant negative correlation with AA (*P* = .06). In subjects with AD, TEWL and the Severity Scoring Atopic Dermatitis (SCORAD) index correlated (*P* < .001). The SCORAD index had a significant correlation with GLA and DGLA (*P* < .001) but not AA (*P* = .06).

**CONCLUSIONS.** AD is associated with a defect in n-6 EFA metabolism. LA metabolites are involved in the maintenance of the epidermal water barrier.

**REVIEWER COMMENTS.** Antimicrobial protein defects, filaggrin defects, and fatty acid defects are among the newer areas of research on the underlying pathogenesis of AD. Because human epidermis lacks the capacity to convert LA to GLA or DGLA to AA, it is likely that these LA metabolites are synthesized elsewhere and transported to the epidermis. Serum levels of n-6 EFAs, as reported here, presumably reflect epidermal concentrations. It follows, therefore, that dietary supplementation of GLA or topical application of LA metabolites may have therapeutic benefit.

**Randomized, Placebo-Controlled Trial of *Lactobacillus rhamnosus* GG as Treatment of Atopic Dermatitis in Infancy

**PURPOSE OF THE STUDY.** To investigate the efficacy of *Lactobacillus rhamnosus* GG (LGG) as a food supplement for children with mild-to-moderate atopic dermatitis (AD).

**STUDY POPULATION.** One hundred two children aged 3 to 12 months with mild-to-moderately severe AD who were not taking antiinflammatory medications were included in this German study.

**METHODS.** Subjects were randomly assigned to receive LGG (5 × 10⁹ colony-forming units twice per day) or placebo for 12 weeks. Severity Scoring Atopic Dermatitis (SCORAD) index and use of hydrocortisone 1% ointment as a rescue medication were recorded at 4, 8, and 12 weeks of treatment.

**RESULTS.** One hundred two subjects were randomly assigned and completed the treatment period (54 in the treatment group, 48 in the placebo group). Initial symptom load was similar in both groups (SCORAD index: 24.6 ± 8.8 in the LGG group and 23.6 ± 7.8 in the placebo group) and improved over time. There were no statistically significant differences between the groups at any of the analysis times (SCORAD index for LGG versus placebo: 23.8 ± 12.4 vs 20.6 ± 9.9 at 4 weeks, 22.5 ± 14.6 vs 17.9 ± 13.1 at 8 weeks, and 19.6 ± 15.4 vs 15.1 ± 12.1 at 12 weeks, respectively). No statistically significant differences were found when the data were stratified according to age, eczema severity, or use of rescue medications, and no differences were found in the use of rescue medications, total immunoglobulin E level, or newly developed allergic sensitization to hen’s egg or cow’s milk.

**CONCLUSIONS.** This study showed no therapeutic effect of LGG for the treatment of mild-to-moderate AD in infancy. **REVIEWER COMMENTS.** In our practice, parents of children with AD frequently inquire about whether they should supplement their children’s diets with lactobacilli. Previous studies had shown some possible benefit of supplementation with lactobacilli for prevention of AD in...
Intermittent Therapy for Flare Prevention and Long-term Disease Control in Stabilized Atopic Dermatitis: A Randomized Comparison of 3-Times-Weekly Applications of Tacrolimus Ointment Versus Vehicle


PURPOSE OF THE STUDY. To examine the usefulness of regular intermittent therapy instead of treating flares for the approach of atopic dermatitis (AD).

STUDY POPULATION. A total of 383 patients were randomly assigned to the stabilization phase, and 288 patients were controlled on tacrolimus ointment. There were 68 children (aged 2–16 years) and 57 adults (>16 years) in the tacrolimus arm and 37 children and 35 adults in the vehicle arm. Eighty-five percent had moderate AD, and 15% had severe AD.

METHODS. Adult and pediatric patients with moderate-to-severe AD who were clear of disease after up to 16 weeks of treatment with tacrolimus ointment were randomly assigned in a double-blind fashion to 3-times-weekly treatment with either tacrolimus ointment (0.03% or 0.1%) or vehicle for 40 weeks. The primary end point was the number of flare-free treatment days. Relapses were treated with open-labeled tacrolimus.

RESULTS. There were 288 patients who entered the randomization phase. The largest reasons for not finishing the stabilization phase were voluntary patient withdrawal for 95 patients and loss to follow-up for 55 patients. Only 16 (4.2%) patients were withdrawn for lack of efficacy. A total of 125 patients were randomly assigned to tacrolimus, and 72 patients were assigned to vehicle. The mean number of flare-free treatment days was 177 for the tacrolimus group and 134 for the vehicle group (P = .003). Median time to first relapse was 169 days for the tacrolimus group and 143 for the vehicle group (P = .037).

CONCLUSIONS. Maintenance therapy with tacrolimus ointment was associated with significantly more flare-free days compared with vehicle and a significantly longer time until first disease relapse.

REVIEWER COMMENTS. This article examined the possibility of proactive treatment of AD instead of reacting to flares.

Sustained Efficacy and Safety of Pimecrolimus Cream 1% When Used Long-term (up to 26 Weeks) to Treat Children With Atopic Dermatitis


PURPOSE OF THE STUDY. To evaluate the efficacy and safety of pimecrolimus cream 1% (Elidel [Novartis, East Hanover, NJ]) used for 26 weeks in children with atopic dermatitis (AD)

STUDY POPULATION. This was a prospective study of 403 children aged 2 to 17 years with AD (mean age at enrollment: 6.7 years) recruited from multiple academic centers in the United States.

METHODS. Pooled data were assessed from 20-week, open-label (OL) extensions of 2 previously reported 6-week, double-blind (DB) phase studies in which patients were randomly assigned 2:1 to pimecrolimus or vehicle. During the OL phase, all patients were treated with pimecrolimus. During the DB phase, no other AD treatments except emollients were allowed. The efficacy parameters included the Investigator’s Global Assessment (IGA), Eczema Area and Severity Index, and severity of pruritus scores. Safety assessment consisted primarily of monitoring adverse events. Patients were evaluated on days 8, 15, 22, 29, 43, 71, 99, 141, and 183.

RESULTS. Overall, 60.3% of the patients had moderately severe AD (IGA: 3) at study entry. Twice as many in the control group discontinued during the DB phase compared with the treated group (25% vs 11.4%). The main reason for the higher discontinuation rate in the control group was unsatisfactory therapeutic effect (15.4% vs 2.6%). Eighty-four percent completed the OL phase with similar rates of completion between the groups. At day 43, 34.8% of the pimecrolimus-treated patients versus 18.4% in the vehicle groups (P < .001) had clear or almost clear (IGA: 0 or 1) disease. Pimecrolimus was significantly more effective (P < .0001) in treating the
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